Peer Review File

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Reviewer A Comments

1. Needle core biopsy is more common than excisional biopsy. Consider add how to assess adequacy and triage for morphology, IHC/molecular tests, and flow cytometry. There is diagnostic pitfall for T-ALL and type B thymoma, especially in needle core biopsy and lock of epithelial components in the biopsy, flow cytometry will show immature T-cells and not all T-ALL cases show aberrant immature T-cell markers. In case like this, TCR gene rearrangement may help. Consider add more discussion and flow cytometry evaluation for T-ALL and thymoma.

Reply 1: Thank you to the reviewer for this comment. The manuscript already includes some information regarding the differential diagnosis between T-ALL and B thymoma in core biopsies. However, we have made some emphasis to the reviewer's points (see changes in text below). Because the target audience of this review are cytologists, surgical pathologists and thoracic pathologists, we did not include too detailed hematopathology information that is not routinely used by these subspecialists. The purpose of this review is to have a general concept of the most characteristic anterior mediastinal hematolymphoid entities and how to first approach/triage them. Then we encourage a hematopathology consultation for refined diagnosis, if needed.

Changes in the text: Page 14, first paragraph, we have included the following sentence (highlighted in red): *"In a small biopsy the diagnostic features of thymoma may not be easily to identify and there may be a paucity of epithelial cells making the histologic distinction with T-LBL challenging. IHC, flow cytometry and/or molecular studies may be of help to further clarify the diagnosis."*
Page 15, second paragraph, we have included the following sentence (highlighted in red): *"If flow cytometry is available, T-LBL is typically composed of an aberrant immature T-cell population and B1 thymoma and normal thymus will show T-cells at various stages of maturation. However, in some instances T-LBL may not show an aberrant immunophenotype by flow cytometry and distinction from normal thymocytes may not be possible. In this instance, close communication with a hematopathologist is needed as to consider the clinical scenario and decide to further perform TCR gene rearrangement to asses for the presence or absence of a clonal T-cell population."*

2. In rare cases, CD30 positive large B-cell lymphoma, may not express common B-cell markers such as CD19, CD20, CD79a, PAX5, may partial express CD45LCA but strong express BOB1/OCT2 and IgH gene rearrangement positive. Consider add more discussion of these rare cases in differential diagnosis of cHD and PM-LBL.

Reply 2: Thank you to the reviewer for this comment. We consider that this instance is quite rare indeed, but agree that this could enter the differential diagnosis of CHL and PM-LBCL. We have included some information about this into the discussion of the differential diagnosis of CHL and PM-LBCL (see changes in text below). Because the target audience of this review are cytologists, surgical pathologists and thoracic pathologists, we did not include too detailed hematopathology information that is not routinely used by these subspecialists. The purpose of this review is to have a general concept of the most characteristic anterior mediastinal hematolymphoid entities and how to first approach/triage them. Then we encourage a hematopathology consultation for refined diagnosis, if needed.

Changes in the text: Page 10, we have included a new paragraph #3 (highlighted in red) with the following information: *"Rarely, cases of CD30+ anaplastic large B-cell lymphoma may lose expression of >1 B-cell marker (CD20, CD79a) and the use of additional B-cell markers (OCT2, BOB.1) may be required to further confirm a B-cell lineage."*

3. Consider add follicular dendritic cell sarcoma in the discussion.

Reply 3: Although this is a good suggestion, we consider that follicular dendritic cell sarcoma is quite distinct morphologically and immunophenotypically to be included in this current review that focuses in the approach/triage of lymphoid processes. Perhaps this topic could be better suited for a review on mediastinal sarcomas or spindle cell neoplasms.

Changes in the text: None.

Reviewer B Comments

CD cell phenotyping combined with morphology assessment is a powerful tool in cancer diagnostics. Authors showed an interesting approach to the analysis by dividing neoplams into age related groups and by doing a DDx in each subgroup based on evaluation concept mentioned above. It is a nice review article with high clinical aspect.

Reply 1: We thank the reviewer for the kind and appreciative comments.

Changes in the text: None requested.